REMARKS

STATUS OF CLAIMS

Claim 15 has been canceled. Claim 18 has been amended for greater clarity. Claims 10, 13, 14, and 16-26 are pending. Support for this claim amendment can be found throughout the specification and in the originally filed claims.

REJECTIONS UNDER 35 U.S.C. § 112, first paragraph

Claims 10, 13, 14, and 16-26 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Applicants contend that one of skill in the art could readily practice the present invention.

Claim 10 (from which Claims 13, 14, and 16-26 depend) is directed to a method for treating an individual suffering from a wound comprising administering an effective amount of a lymphotactin (XCL1) to the individual, whereby administration of the lymphotactin (XCL1) accelerates wound healing.

Regarding the allegation that the specification "does not hypothesize what role XCL1 plays in wound healing (*e.g.*, enhances reepithelialization, growth factor for fibroblasts, *etc.*)," Applicants point out that, "an inventor need not know how or why his or her invention does work in order to obtain a patent." Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1375 (Fed. Cir. 1999), citing Newman v. Quigg, 877 F.2d 1575 (Fed. Cir. 1989). Consequently, Applicants do not need to understand how XCL1 accelerates wound healing to obtain a patent, but rather only that this is the end result.

Applicants disagree that Hedrick *et al.* (U.S. Patent 6,022,534) teach against administering XCL1 to enhance cell growth, such as is desirable at a wound. Rather, Hedrick *et al.* do not address whether XCL1 activity is desirable to promote wound healing.

Hedrick *et al.* teach that XCL1 increases the number of various lymphocytes either by attracting cytotoxic T lymphocytes (CTL) and/or natural killer cells (NK), and/or inducing proliferation of resident cells. (Hedrick *et al.*, col 2, lines 17-22). In particular, increasing the number of such lymphocytes at a location where there are tumor cells in an animal is preferred. (Hedrick *et al.*, col 2, lines 44-54).

Hedrick *et al.* also teach that "an antagonist will be effective in preventing the recruitment of such cells. This may be important, *e.g.*, in a transplantation context, where NK and/or CTL function is harmful." (Hedrick *et al.*, col 2, lines 30-34).

Hedrick *et al.*, thereby suggest the local environment dictates whether XCL1 activity is or is not desirable.

The following articles (abstracts of which are enclosed herein) support the nexus between XCL1 activity and wound healing.

- Boismenu *et al.*, "Chemokine expression by intraepithelial gamma delta T cells. Implications for the recruitment of inflammatory cells to damaged epithelia" *J Immunol*, **157(3)**:985-992 (1996).
  XCL1 was shown to be inducible in dendritic epidermal T cells (DETC) 7-17 and the most abundant chemokine produced by activated DETC 7-17 cells (amongst those examined MIP-1alpha, MIP-1 beta, and RANTES). Similarly, copious amounts of XCL1 mRNA was produced by activated primary DETC cultures as well as activated freshly isolated intestinal intraepithelial T cells (I-IEL) (with T cells expressing gamma delta). Migration of CD8+ T cells induced by culture supernatants from stimulated DETC 7-17 cells (which contain XCL1) was strongly reduced in the presence of neutralizing anti-XCL1 antiserum. Authors suggest gamma delta IEL play a role in the maintenance of epithelia homeostasis.

- Huang *et al.*, "Neutrophils and B cells express XCR1 receptor and chemotactically respond to lymphotactin," *Biochem Biophys Res Commun*, **281(2)**:378-382 (Feb 2001).
  XCL1 shown to be chemotactic for B lymphocytes and neutrophils as well as T lymphocytes. In addition, expression of XCR1 (the receptor for XCL1) found only in association with these cells. Authors suggest that XCL1 plays a key role in the regulation of T and B lymphocytes, and neutrophil trafficking, and thereby their roles in inflammatory and immunological responses.

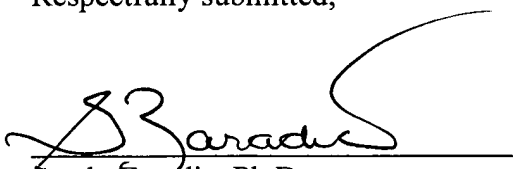
In view of the guidance available at the time of filing, for example, as noted above, Applicants submit that undue experimentation would not be required to practice the present invention as defined by the amended claims. Additional support for how to administer XCL1 to accelerate wound healing can be found throughout specification, for example, on page 11, line 14 to page 12, line 2as well as on page 14, line 1 to page 17, lines 26.

In light of the above arguments, Claims 10, 13, 14, and 16-26 are believed to be enabled by the specification. As such, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

CONCLUSION

It is believed that the foregoing amendment places this application now in condition for allowance. Therefore, favorable action allowing pending Claims 10, 13, 14, and 16-26 is respectfully solicited.

Respectfully submitted,



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1: J Immunol. 1996 Aug 1; 157(3): 985-92.

Chemokine expression by intraepithelial gamma delta T cells. Implications for the recruitment of inflammatory cells to damaged epithelia.

Boismenu R, Feng L, Xia YY, Chang JC, Havran WL.

Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037, USA.

T cells expressing gamma delta TCR may have evolved to recognize Ag in a different manner as well as perform a broader set of functions than T cells with alpha beta TCR. In this study, we tested the hypothesis that dendritic epidermal T cells (DETC) bearing the invariant V gamma 3V delta 1 TCR may be able to signal the migration of peripheral alpha beta T cells to the epidermis by secreting specific chemokines. Expression of macrophage inflammatory protein (MIP)-1 alpha, MIP-1 beta, RANTES, and lymphotactin was inducible in DETC 7-17 cells, whereas mRNA for monocyte chemoattractant protein (MCP)-1 could not be detected. Strikingly, lymphotactin was the most abundant chemokine produced by activated DETC 7-17 cells. Activated primary DETC cultures also produced copious amounts of lymphotactin mRNA. Similarly, freshly isolated and activated intestinal intraepithelial T cells (i-IEL) with gamma delta TCR expressed high levels of lymphotactin mRNA. In contrast, lymphotactin mRNA was present in activated spleen gamma delta T cells at low basal levels. Migration of CD8+ T cells induced by culture supernatants from stimulated DETC 7-17 cells was strongly reduced in the presence of a neutralizing anti-lymphotactin antiserum and to a lesser extent by neutralizing anti-MIP-1 alpha, anti-MIP-1 beta, or anti-RANTES antiserum. The presence of lymphotactin in supernatants from activated DETC 7-17 cultures was directly demonstrated by Western blot analysis. These observations are consistent with a model in which gamma delta IEL play an active multi-faceted role in the maintenance of epithelia homeostasis.

PMID: 8757601 [PubMed - indexed for MEDLINE]

1: Biochem Biophys Res Commun. 2001 Feb 23; 281(2): 378-82.

ELSEVIER
FULL-TEXT ARTICLE

Neutrophils and B cells express XCR1 receptor and chemotactically respond to lymphotactin.

Huang H, Li F, Cairns CM, Gordon JR, Xiang J.

Department of Microbiology, College of Medicine, Saskatoon Cancer Center, University of Saskatchewan, Saskatoon, Saskatchewan S7N 0W0, Canada.

The C chemokine lymphotactin (Lptn) has been reported to act specifically on CD4(+) and CD8(+) T lymphocytes and natural killer (NK) cells, but not monocytes. However, the chemotactic effect of Lptn on other types of hematopoietic cells has not been well studied. In this study we investigated (i) the chemotactic influences of Lptn on T and B lymphocytes, neutrophils, monocytes, and dendritic cells, and (ii) the expression of the Lptn receptor (XCR1) by these cells, using RT-PCR. Our data showed that Lptn is chemotactic for B lymphocytes and neutrophils as well as T lymphocytes, but not for monocytes or dendritic cells, and that XCR1 expression is found only in association with T and B lymphocytes and neutrophils, but not monocytes or dendritic cells. Thus, this study is the first demonstration of a chemotactic effect of Lptn on neutrophils and confirms the association of this effect with expression of the XCR1 receptor on these cells. These data suggest that Lptn could potentially be an important protein in the regulation of T and B lymphocytes and neutrophil trafficking, and thereby also their roles in inflammatory and immunological responses. Copyright 2001 Academic Press.

PMID: 11181058 [PubMed - indexed for MEDLINE]